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| 10/617,910 | 07/10/2003 | Gillian Daphne Elliott | 5759-66308-01 | 4218 |

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| EXAMINER | |
|---|---|
| LUCAS, ZACHARIAH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/617,910 | ELLIOTT, GILLIAN DAPHNE | |
| | Examiner | Art Unit | |
| | Zachariah Lucas | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12-16* is/are pending in the application.

4a) Of the above claim(s) *13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/381,211.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-10-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I (methods of delivering a substance to microtubules comprising exposing the substance coupled to a herpesviral VP22 protein, to microtubules) and to species (A) (wherein the substance is fused to the VP22 polypeptide) in the reply filed on January 12, 2005 is acknowledged. The traversal is on the ground(s) that there would be no undue burden in the examination of all the claims of Group I and Group II. This is not found persuasive because the claims of Group I are drawn to a method of using a compound whereas the methods of Group II are drawn to methods of making the compound. However, the compounds used in Group I may be made by other means than those identified in Group II. For example, Group II requires to fusion or other coupling of the substance to be delivered to the VP22 protein. However, because Group I reads on a method of exposing the compounds to microtubules, they would also read on the use of compounds made by any means, not according to any specific method. Because a search for the methods of making would therefore not be coextensive with the search for methods of using, the Applicant's arguments in traversal are not found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 13-16 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 12, 2005.

***Priority***

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to the United Kingdom application 9705903.4, filed on March 21, 1997. The certified copy has been filed in parent Application No. 09/381,211, filed on September 17, 1999 (a national stage entry of PCT/GB98/00873 filed on March 23, 21998).

***Information Disclosure Statement***

4. The information disclosure statement (IDS) submitted on July 10, 2003 in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

5. It is noted that the reference to Elliott et al, Cell 83: 223-33 (1997) in the IDS appears as though it should cite to Volume 88, not 83, of the journal.

6. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

WO 93/02065

7. The following reference was provided only in the form of a foreign language document without an English language translation or statement as to why it was considered relevant. As such, the citation does not comply with 37 CFR 1.98. The reference has therefore been crossed off from the IDS reference listing as it was not properly submitted, and has therefore not been considered.

EP 0524093

***Specification***

8. The disclosure is objected to because of the following informalities: the term "concnern" on line 9 of page 9 appears as though it should read - - concern- -.

Appropriate correction is required.

### *Claim Objections*

9. Claim 12 is objected to because of the following informalities: a comma should be inserted between the phrases "a covalent coupling" and "and a non-covalent association" in line 3 of the claim. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on a method of delivering a substance to a microtubule comprising exposing the substance to the microtubule, wherein the substance is couple to a herpesviral VP22 protein or a portion thereof having "a" microtubule binding function of VP22. The use of the term "a microtubule binding function" implies that there are multiple such functions. However, the application discloses only the generic microtubule binding function of the protein. It is therefore unclear what is meant by "a microtubule binding function" as only one such function has been disclosed.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim describes the use of a genus of inventions comprising any portion or derivative of a herpesviral VP22 polypeptide "which has a binding function of VP22."

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present application, the Applicant has disclosed that the entirety of the VP22 protein binds to microtubules, and that certain truncated forms thereof are, or are not, able to bind to them. Page 15. However, while the reference identifies both fragments that are and are not able to bind to microtubules, the application is not clear as to which specific region(s) of the protein are required for microtubule binding. See e.g., page 15, lines 21-24 (indicating that residues between amino acid positions 119 and 192 may be involved in microtubule binding, or that deletion of these residues may merely result in a disruption of the overall VP22 structure so as to prevent such binding). In this case, the presentation of a few species is not sufficient to demonstrate possession of the claimed genus, because it is not clear from these species what the full scope of the claimed genus is. Further, because it is not clear from that application what residues comprise the minimum region(s) required for microtubule binding, and because there is no other identification of any structure that correlates to the ability of VP22 to bind to microtubules, the application has not provided any means of identifying the claimed genus other than by function. As function alone is not sufficient to provide descriptive support for a genus (see, the MPEP excerpt above), the application has not provided adequate support for the claimed invention.

Additionally, the application has established only that the VP22 protein of the herpes simplex virus 1 are able to bind microtubules. However, the claims are drawn to any herpesvirus VP22 proteins, or portions or variants thereof. It is known in the art that the term "herpesvirus" includes a number of viruses, including HSV1. See e.g., definition of "herpesvirus" in the On-Line Medical Dictionary, and the entry for "Herpesviridae" in the MeSH Browser. However, while the claims are broadly drawn to the VP22 protein of any herpesvirus, there is no

demonstration that this function is common to all herpesvirus proteins. Further, the teachings in the art indicate that the microtubule binding function of the HSV1 VP22 is relatively rare. See e.g., Elliott et al., Cell 88: 223-33, abstract (stating "VP22 utilizes a *novel* trafficking pathway that involves the actin cytoskeleton" [*emphasis added*]). Because the Applicant has not demonstrated that any VP22 from any herpesvirus would share the ability of the HSV1 protein to bind microtubules. Further, because it is not clear what structure within the HSV1 protein permits this activity, it cannot be determined with any certainty which of the other herpesvirus may or may not share this activity.

For these reasons, the Applicant has not provided adequate support for methods of using any herpesvirus VP22 construct to deliver a substance to microtubules in a cell.

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by either of WO 97/05265 or Elliott et al. (Cell 83:223-233). Both of these references have been made of record in the IDS of July 2003. This claim reads on a method of delivering a substance to microtubules by exposing the microtubules to the substance wherein the substance is in the form of a fusion with a herpesvirus VP22 protein. The specification of the present application teaches that VP22

binds microtubules. Page 2, lines 10-12. Because the binding of microtubules is an inherent property of the VP22 protein, the introduction of any VP22/substacen fusion into a cell would inherently perform the claimed method.

Each of the cited references teach a method wherein a VP22 variant is transported among cells to deliver a substance into cells other than the cell of origin. CO 97/05265, pages 14-17; and Elliott, pages 228-29. The variants comprised a fusion of the VP22 protein and an inserted antibody epitope (a substance). This substance was found to be transported among cells in the described method. Because the VP22 protein inherently binds microtubules, and that protein was used to transport the substance as described in the references, the processes described in the references inherently anticipate the claimed method.

***Double Patenting***

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-8 of U.S. Patent No. 6184038. Although the conflicting claims are not identical, they are not patentably distinct from each other because the

claims of the present application represent are generic to the claims of the patent. In particular, claim 8 of the patent reads on methods of delivering a compound to a cell through delivering to the cell a conjugate of a herpesviral VP22, particularly those disclosed in the patent as SEQ ID NOs: 1 or 2, and the compound to be delivered. SEQ ID NOs: 1 and 2 are disclosed in the patent as the full length, and the Δ267 mutant, versions of VP22. Each of these versions of VP22 is disclosed in the present application as binding to microtubules. Page 15. Because the patent claims a method of delivering a substance to a cell by conjugating it to the VP22 proteins of SEQ ID NOs: 1 or 2, and because these proteins inherently bind to microtubules, then the claims of the patent inherently read on the presently claimed method. Because the claims of the patent would anticipate the current claim if applied as prior art, the current claim 12 is rejected for obviousness type double patenting over the patent claims.

18. Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16 of U.S. Patent No. 6017735. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present application represent are generic to the claims of the patent. The present claim has been described above. Claim 16 of the patent describes a method of transporting a first polypeptide into a cell population comprising exposing the cells to a fusion polypeptide comprising a first polypeptide (the substance to be delivered) and a second, VP22, polypeptide, which may be the full length VP22. Because VP22 would inherently, upon transporting the substance into the cells, also bind to the microtubules, and thereby deliver the substance to the microtubules, the claim of the patent inherently reads on the presently claimed method. Because

the claims of the patent would anticipate the current claim if applied as prior art, the current claim 12 is rejected for obviousness type double patenting over the patent claims.

19. Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 6251398. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present application represent are generic to the claims of the patent. The present claim has been described above. Claim 10 of the patent describes a method of transporting a first polypeptide into a cell population comprising exposing the cells to a fusion polypeptide comprising a first polypeptide (the substance to be delivered) and a second, VP22, polypeptide, which may be the full length VP22. Because VP22 would inherently, upon transporting the substance into the cells, also bind to the microtubules, and thereby deliver the substance to the microtubules, the claim of the patent inherently reads on the presently claimed method. Because the claims of the patent would anticipate the current claim if applied as prior art, the current claim 12 is rejected for obviousness type double patenting over the patent claims.

***Conclusion***

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C Housel 2/18/05

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